

# METHODS FOR MAGNETIC RESONANCE ANALYSIS USING MAGIC ANGLE TECHNIQUE

## STATEMENT OF GOVERNMENT SUPPORT

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## FIELD

The present disclosure relates to magnetic resonance (MR) analysis, particularly to magnetic resonance spectroscopy (MRS) and imaging (MRI) of biological objects.

## BACKGROUND

Magnetic resonance is a phenomenon exhibited by a select group of atomic nuclei and is based upon the existence of nuclear magnetic moments in these nuclei (termed "gyromagnetic" nuclei). When a gyromagnetic nucleus is placed in a strong, uniform and steady magnetic field (a so-called "external field" and referred to herein as a "static" magnetic field), it precesses at a natural frequency known as a Larmor frequency. The Larmor frequency is characteristic of each nuclear type and is dependent on the applied field strength in the location of the nucleus. Typical gyromagnetic nuclei include  $^1\text{H}$  (protons),  $^{13}\text{C}$ ,  $^{19}\text{F}$  and  $^{31}\text{P}$ . The precession frequencies of the nuclei can be observed by monitoring the transverse magnetization that results after a strong RF pulse applied at or near their Larmor frequencies. It is common practice to convert the measured signal to a frequency spectrum by means of Fourier transformation.

More specifically, when a bulk sample containing nuclear magnetic resonance (NMR) active nuclei is placed within a magnetic field, the nuclear spins distribute themselves amongst the nuclear magnetic energy levels in accordance with Boltzmann's statistics. This results in a population imbalance between the energy levels and a net nuclear magnetization. It is this net nuclear magnetization that is studied by NMR techniques.

At equilibrium, the net nuclear magnetization is aligned parallel to the external magnetic field and is static. A second magnetic field perpendicular to the first and rotating at, or near, the Larmor frequency can be applied to induce a coherent motion of the net nuclear magnetization. Since, at conventional field strengths, the Larmor frequency is in the megahertz frequency range, this second field is called a "radio frequency" or RF field.

In particular, a short (microsecond) pulse of RF radiation is applied to the sample in the static magnetic field; this pulse is equivalent to irradiating at a range of frequencies. The free induction decay (FID) in response to the RF pulse is measured as a function of time. The response of the sample to the pulse depends upon the RF energy absorption of the sample over a range of frequencies applied (for example, 500 MHz $\pm$ 2500 Hz). Often the pulse is applied many times and the results are averaged to improve the signal-to-noise ratio.

The coherent motion of the nuclear magnetization about the RF field is called a "nutation." In order to deal conve-

niently with this nutation, a reference frame is used which rotates about the z-axis at the Larmor frequency. In this "rotating frame" part of the RF field, which is rotating in the stationary "laboratory" reference frame in the same direction as the magnetization, is static. Consequently, the effect of the RF field is to rotate the nuclear magnetization direction at an angle with respect to the main static field direction. By convention, an RF field pulse of sufficient length to rotate the nuclear magnetization through an angle of 90° or  $\pi/2$  radians is called a " $\pi/2$  pulse."

A  $\pi/2$  pulse applied with a frequency near the nuclear resonance frequency will rotate the spin magnetization from an original direction along the main static magnetic field direction into a plane perpendicular to the main magnetic field direction. The component of the net magnetization that is transverse to the main magnetic field precesses about the main magnetic field at the Larmor frequency. This precession can be detected with a receiver coil that is resonant at the precession frequency and located such that the precessing magnetization induces a voltage across the coil. Frequently, the "transmitter coil" employed for generating the RF field to the sample and the "receiver coil" employed for detecting the magnetization are one and the same coil.

In addition to precessing at the Larmor frequency, in the absence of the applied RF field, the nuclear magnetization also undergoes two relaxation processes: (1) the precessions of various individual nuclear spins which generate the net nuclear magnetization become dephased with respect to each other so that the magnetization within the transverse plane loses phase coherence (so-called "spin-spin relaxation") with an associated relaxation time,  $T_2$ , and (2) the individual nuclear spins return to their equilibrium population of the nuclear magnetic energy levels (so-called "spin-lattice relaxation") with an associated relaxation time,  $T_1$ . The spin-spin relaxation is caused by the presence of small local magnetic fields, arising from the electrons, magnetic nuclei, and other magnetic dipoles surrounding a particular nucleus. These fields cause slight variations in the resonance frequency of the individual nuclei, which results in a broadening of the NMR resonance line. Often this broadening is caused by two types of local fields: a static component, which gives rise to a so-called inhomogeneous broadening, and local fields which are fluctuating in time as a result of molecular motions and interactions between magnetic nuclei. The latter phenomenon results in a so-called homogeneous broadening.

Magnetic resonance imaging and magnetic resonance spectroscopy are used extensively in biological research and medicine, both for in vitro investigations of cells and tissues and for in vivo measurements on animals and humans. Both methods are non-invasive and non-destructive and are used for a large variety of applications, including the detection and diagnosis of lesions and diseases, and the evaluation of therapy response. One particularly useful MRS technique is  $^1\text{H}$  nuclear magnetic resonance (NMR) spectroscopy.  $^1\text{H}$  NMR spectroscopy has been used extensively to study metabolic changes in diseased cells and tissues and the effects of therapy. The resonance lines corresponding to several key mobile compounds have been observed, and their spectral intensities have been linked to the tumor phenotype, tumorigenesis, tumor size, increased proliferation of cells, cell apoptosis, and necrosis.

However, a serious typically problem associated with these applications is the relatively large widths of the MR resonance lines that are observed using conventional MRI and MRS. This reduces the MRI and MRS sensitivity, and, for MRS, can result in severely overlapping spectral lines, which can impede the analysis of the spectrum. It has been estab-